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DISEASES OF THE NERVOUS SYSTEM

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

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DISEASES of the NERVOUS SYSTEM

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

Psychiatry and Medicine — One and Inseparable

CHARLES BURLINGAME, M.D.*
Hartford, Connecticut

If I had attempted to write on this subject two or three years ago, it would have been much more provocative. So much water has gone over the dam in the past few years that it is much less of a controversial subject than it would have been in 1947. For a while it looked as if the medical profession was going to find us drifting more toward theology and sociology than toward our conventional concepts of medicine.

I intend no disparagement when I say that we should take a good look at ourselves and decide first what our primary responsibilities are as a specialized branch of medicine and what our ancillary responsibilities are. To illustrate: we all recognize the fact that the surgeon must employ not only his exclusively surgical skills but also certain helpful procedures which are not in reality a part of surgery.

A better example would be in the field of tuberculosis. The men in this field have done yeomen's work in establishing the pathology of tuberculosis and its treatment and then have taken on the ancillary responsibilities of preventing tuberculosis through educating the people, through preaching good home construction, good feeding, balanced diets, and all that. But I feel certain that the progress made in tuberculosis would not have been made if our brethren in that specialty had dropped the responsibility for treating the people ill with tuberculosis, had forsaken their laboratories and gone out to beat the drums and try to popularize.

The basis of the popularization of tuberculosis was solid accomplishment; upon that basis, as an ancillary but nevertheless important part of the tuberculosis specialty, came the interesting of lay groups in doing these ancillary things. If we will stop and think about tuberculosis, we will see that it has a distinctly sociological side, an economic side, a political side. But certainly the specialists in tuberculosis would never have got anywhere if they had tried to run the politicians and take their job away from them, if they had tried to take over the housing projects and run them, or tried to take over the economic side and run that. In other words, it is because the tuberculosis men worked in their laboratories, worked on their sick people, and used that as their primary responsibility—always keeping in mind that that was their exclusive riding-field—that the progress has been made in the field of tuberculosis.

I think that we might now take a good frank look at ourselves in the field of psychiatry. Having formerly been largely confined to mental hospitals, and venturing out only with much temerity, we suddenly have found ourselves the "popular gals at the ball." In our new-found prominence, we have done just a little bit too much strutting, possibly. We have been just a bit too glib with the promises, and, most important of all, we have talked about the "broader vision" in the field of psychiatry. I am not sure that we have always been wise or dis-

*Psychiatrist-in-Chief The Institute of Living.
Presented at the Annual Meeting of the Southern Psychiatric Association, November 29, 1949, New Orleans, Louisiana.

creet in talking about this so-called "broader vision." There are very few among us who, although excellent clinicians and therapists in all lines, would be cut out by native endowment, training, and interest to handle the "broader vision" if we had the opportunity. To be sure, these so-called broader problems and broader views in psychiatry are dazzling. It is a temptation to all of us to let ourselves be distracted by them from the hard-headed, unromantic work of the day, wrestling with the problems of individual patients.

But therein lies our danger. Our first and foremost responsibility is to the sick person, and all of these other things which we are likely to refer to as the "broader vision" are ancillary. I have no quarrel whatsoever with those who are pointing out the ancillary possibilities. I think it is a fortunate thing that they are being pointed out, but our thinking must not get out of balance. We must dignify and emphasize the fact that the greatest possible gain in the field of psychiatry will stem from the better care of the individual patient.

And now I shall divide the remainder of my remarks between two considerations. First, I might ask a question: Are we right now suffering from an international case of jitters? Is the anxiety greater than it has been at previous times? Or is this just the aftermath of a war?

I have asked these questions during the past few months, of groups prominent in the newspaper world, groups prominent in the financial, the political, and the industrial worlds. The members of all these groups answer in unison that there is a bad case of anxiety jitters and irritability. To make a long story short, all of them are aware that people are on edge, that there is a great explosive quality in their anxiety and that this anxiety extends to all walks of life; that it is influencing the individuals in their employ, and individuals who are dealing with them; and that their business is being oriented to handle the anxiety.

We as psychiatrists sometimes think that we are the smart boys who know all about the human emotions and are able in diagnosing them. Yet I wonder how many in our midst have totally ignored this basic consideration which these business men and business groups seem to appreciate and analyze so accurately. How many of us are at the present moment able to diagnose and size up the milieu in which the human fish is swimming today and compare it with the milieu in which he swam a year ago or 10 or 20 or 30 years ago? And yet that is the basic consideration if we are to understand the human fish himself, his inability to meet life, and his mental breakdowns. We must be able to understand this change in the milieu that our human fish is going back to swim in after we have treated him; and we must understand it so well that we can prepare him thoroughly to do this new changing and adapting to the milieu.

"But," you say to me, "you have just raised the question as to whether the doctor shouldn't stay on his job." I raised the question as to whether or not it was our job to try to control, to take all the ancillary responsibilities. I do not wish to imply that it is our responsibility to liquidate this international case of jitters. We can't do it.

There isn't a Chinaman's chance that, if we were invited to examine the heads of all the heads of states, as was suggested, that we could do it. In the first place, I don't think there's a Chinaman's chance that we'll ever be invited to examine the heads of states. In the second place, if we were I don't think we'd know how to examine them. In the third place, I might say that if we examined them I don't know how we could treat them. And in the fourth place, the question might well be raised as to who is going to examine the heads of the psychiatrists who examine the heads of the heads of states!

But back again to the differentiation between *understanding* the milieu to which our human fish must return and in which he may have collapsed, and *being responsible for changing* the milieu. It is our responsibility to get this type of a broader vision, and to understand these sociological factors that come to bear upon our patients, exactly the same as it is the responsibility of the tuberculosis specialist to understand that working under poor industrial condi-

tions with dust, poor light and poor food, is a cause of the condition, and to individually make the best adjustment possible within his means or teach the patient so to do.

If I may comment for a moment upon this change of the milieu in which the human fish is now breaking down, I want to say this:—this is not the first time in history that there have been wars and national upheavals and people have found that there is little solid ground under their feet. It is not the first time that the sands have been shifting, and the industrial and financial picture is not what it used to be. The political upheavals have not been altogether dissimilar at different times in history, but there are some very basic differences that I call to your attention, which I am unable to find ever before obtained in modern history.

First, never before has there been an organized effort insidiously to pit group against group. Never before has there been such an organized effort to deprive man of his own pride in industrial accomplishments, with rewards being associated closely with his own effort. Never before has there been a situation where a man's very survival through his job depended on two bosses far removed from his own efforts. I refer to the leaders in the unions as being one group to whom he is responsible, and his conventional employer the other; only too often to date, the interests of these two "bosses" have been diametrically opposed. May the Lord speed the day when this schizophrenic incentivation of the employee may be worked out with justice to the employee!

There has never been a time when in an organized way there was an attack upon a basic consideration which more than any other has helped man in his *travail* and his *extremis*. I refer to religion. I presume that I would not be classed as an overly religious person and yet we in the field of psychiatry must realize that since the beginning of time man has had to have some religious schooling, training, and ideals which he could turn to and which would tide him over. Be this weakness or strength, it has been indispensable. Never before has there been the organized effort that exists today to deprive man of the stabilizing effect, the tranquillizing effect, that has come through religion.

While it is not our job to wind up the universe and solve all these problems, it is our job to get this type of broader vision, and I might say that this kind of broader vision is most important to all branches of medicine.

I want now to point out that there is no such thing as mental diseases *per se*. And I might say that there is no such thing as physical disease *per se*. There is only disease. I do not believe that there is such a thing as having any physical illness without some psychological accompaniment.

I might here describe to you a concept which has clarified my own thinking.

I ask you to imagine a rectangle in which we are to incorporate all of disease. From the lower left-hand corner to the upper right-hand corner we will draw a line. Below the line we will say we have the somatic symptoms of disease, and above the line the psychological symptoms. Let us place various diseases and injuries within the rectangle in positions to designate the relative importance of the somatic and the psychological elements in the presenting symptoms. We might place a fracture at the extreme right, where perhaps 90% of the presenting symptoms would be in the field of the soma and 10% above the line in the field of the psyche. I do not believe any of us would debate the question as to whether there is that much psychological accompaniment to a fracture. And then a little farther in we might place a carbuncle, with a certain percentage below the line in the field of the soma and the balance above the line in the field of the psyche. If you don't believe that a carbuncle will change your psychological processes and your personality, at least temporarily, I recommend that you get one.

Not so many years ago, we might with clear conscience have placed any number of diseases and disorders either entirely above or entirely below the line. It was not too long ago that general paresis, for example, was considered entirely a psychological affection. Today, of course, we know of its

relation to syphilis, and would place it near the center of our rectangle, with its presenting symptoms about 50% above and 50% below the line. I could continue with a procession of diseases, but I am sure what I am driving at is evident—that, even as no vertical line can be drawn through the rectangle without passing through both the field of the psyche and the field of the soma, neither can we today find any disease which does not affect both fields. On the psychological side, we have still a whole basketful of conditions heretofore classified as mental diseases, whose somatic accompaniments we are only beginning to understand. But each new discovery seems to drive home the certainty that it will not be long before we take it as a matter of course that the whole man is affected by each disease and trauma.

Moreover, I do not believe there is such a thing as a purely functional disease in the sense that there is no somatic recording. You do not see this page unless there is a recording somewhere in your soma. You don't hear unless there is a recording of some kind in your soma. The facts seem to be that only when the somatic recording is of sufficient intensity or sufficiently protracted can we refer to the condition as disease. And then we might add that that somatic recording can be referred to as disease only when it is of a nature to interfere with the proper functioning, broadly conceived, of the organism.

The mental disease—again a descriptive term—is now being attacked from the laboratories. Reviewing, for example, the last twelve months: along came Casperson and called to our attention the fact that emotional factors would permanently alter the protein metabolism of the nerve cells. And then we find in this same year that Egas Moniz and Hess of Switzerland have been the ones chosen to divide the Nobel Prize. It is an astonishing thing that, in the whole field of medicine, these two men who have been working in the field of psychiatry and neurology have been chosen. Something is happening there which is now being recognized not only by the field of psychiatry but by the whole scientific world.

And only a matter of days ago, our own Dr. Stanley Cobb presented the Salmon Lectures at the New York Academy of Medicine. At that time, he gave three good, hard, scientific addresses. I was a little bit nervous when I heard the first one; the room was filled, but it usually is filled at the first Salmon Lecture. It was hard, scientific fact based upon the microscope and the scientific laboratory. But it was inspiring to see that his audience was equally large on the second night and the lecture was equally hard-headed, scientific, laboratory reporting. The most inspiring thing was that on the third night he had the heaviest audience of all and it was still hard-headed coupling up of the human body with the human mind and its emotions. Dr. Cobb's addresses were styled, "The Anatomy and Physiology of the Human Emotions."

So it would be a stupid person who would any longer debate whether or not psychiatry belonged tighter and tighter in the field of scientific medicine. All of the work, moreover, has tended to show that the emotions have an effect upon the soma and that there is a somatic recording. The present indications are also that psychotherapy has a valid basis in science which will be demonstrated by laboratory findings. "Words have power to heal and power to destroy" seems to be a scientific fact. The use of words in therapy, the play and interplay of one personality upon another, seems to be growing in significance through the demonstrations of the laboratory.

It is for psychiatry to move forward in all huminity, reassured by the fact that the pure science laboratories and other branches of medicine have now accepted us as part of the medical family. As such, I am sure that we will welcome the opportunity to listen as well as contribute to the other branches of medicine in the solving of the greatest public health problem of today. The solution is not going to come through propaganda. It is coming through more workers in the vineyards, striving for the answers, seeking to heal, and humble in the knowledge of the unknown still stretching out ahead of them, but inspired by the accomplishment made in just these few short years.

Phenacetylurea—Phenurone—in Epilepsy*

DOUGLAS T. DAVIDSON, JR., and
WILLIAM G. LENNOX
Boston, Massachusetts

Use of the currently proven and available anti-epileptic drugs singly or invarious combinations fails to control the attacks of a certain number of epileptic patients. We have used a new drug, phenacetylurea (phenurone) in a series of 178 patients, all belonging to this resistant group. The report that follows deals with the experiences gleaned from the first fourteen months of clinical trial.

Phenacetylurea (trade name Phenurone) was developed in the research laboratory by Everett and Richards[1] who found it effective as an anticonvulsant in mice and rabbits. In small animals ataxia was present with an oral dose of 0.4 gm. per kilo, light sleep with 0.8 gm. and death occurred with from .0 to 5.0 gm. per kilo. It was destroyed rapidly by the liver, the anticonvulsant effectiveness being lost after three or four hours. Pathology of liver, kidney or blood was not encountered in animals fed the drug for more than 11 months.

Two reports of clinical use of phenacetylurea have appeared. Gibbs, Everett, and Richards[2] found that approximately one-half of 90 patients treated by them fared better than with any previous medication. Psychomotor seizures were especially well controlled. The most serious side effect was bizarre or even psychotic behavior in persons predisposed in that direction. The therapeutic results reported by Zeifert[3] in a group of 13 patients were much the same. His observations are especially important for the laboratory tests employed, a subject to be discussed later.

Clinical Material and Methods

Patients were those attending the Seizure Clinics of the Children's Medical Center, or private patients of the authors. Three-fourths were children. Seizures had been present for from four months to 30 years. Of the 178 persons treated, 98 had but one seizure pattern, 74 had a combination of patterns and in four the seizure could not be placed in any of the three common groups.

Electroencephalograms were made of all patients. Roentgen studies (including pneumoencephalogram) and other laboratory examinations were made when specifically indicated. As previously stated, phenacetylurea was given only when seizures were uncontrolled by standard anti-epileptics and when patient or parents were agreeable to the use of an experimental drug. Whenever feasible, phenacetylurea was given alone. However, when other medication had proved partially effective over a long period and the seizure frequently was fairly well documented, it was added to the previous medication. Events proved that as a rule best results were obtained when phenurone supplemented the action of another drug or drugs. All but infants were given an initial dosage of 0.25 to 0.5 gm. twice daily for a period of two weeks in order to test susceptibility to side effects. If none appeared, the amount was increased at intervals until control of seizures was attained or toxic symptoms arose. The therapeutic dose depended on the requirements and tolerance of each individual. In children, this amount was from 0.5 to 2.0 gm. daily and for adults from 0.5 to 3.5 gm. Unless seizure frequency or severity was appreciably reduced after a four to eight weeks trial with the tolerated doses, phenacetylurea was discontinued. Patients were informed of the common side effects and told to report immediately any toxic symptoms. They were asked to report at least once each month regarding the therapeutic and the side effects of the medicine. Blood examinations made at monthly intervals measured the hemoglobin and the number and differential count of white corpuscles. Other laboratory

*From the Children's Medical Center, Boston. Read before the Fourth International Congress of Neurology in Paris, Sept. 8, 1949. This is No. LVII in a series "Studies in Epilepsy." Aid was received from the Rockefeller Foundation and the U.S. Public Health Service.

examinations were made for specific indications.

Results

Of the 178 patients given phenacetylurea, either alone or in combination, 49 percent reported sustained improvement in seizure control above results secured with other medication (Figure 1.) Three percent of all patients were seizure free. In 22 percent, improvement was estimated to be more than 50 percent. The effect of medication could not be evaluated in 22 percent of the group because either the period of observation was too short or because the patients did not report. Eleven percent were not improved despite adequate trial and in three percent seizures were more frequent or severe. Fifteen percent stopped medication because of unpleasant side effects. Some of these patients, especially those who developed a rash, had experienced abrupt reduction or cessation of attacks. The seizure control in this last group of 15 percent was not included in the tabulation shown (Figure 1).

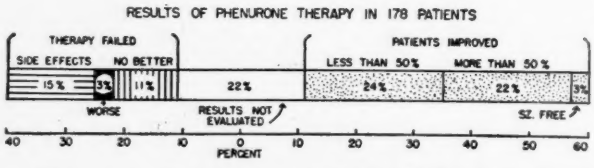

Figure 1. The results of phenacetylurea therapy in 178 patients. The dotted portions of the bar to the right of the scale denotes the percentage who were improved. To the left of the scale are those for whom the therapy failed, although some of those who stopped treatment because of side effects had experienced fewer seizures.

Experience has shown that a certain medicine may be especially effective for a certain kind of seizure. The relationship between the type of seizure and success of phenacetylurea therapy is shown graphically in Figure 2. Following is the proportion of patients in each group who experienced an improvement of at least 50 percent in the frequency of seizures; psychomotor seizures only, 43 percent; petit mal only, 37 percent; grand mal only, 33 percent; a combination of grand mal and psychomotor, 30 percent; and a combination of grand and petit mal, 19 percent. The number of patients in each group appears in Figure 2.

Seizure control was less successful when

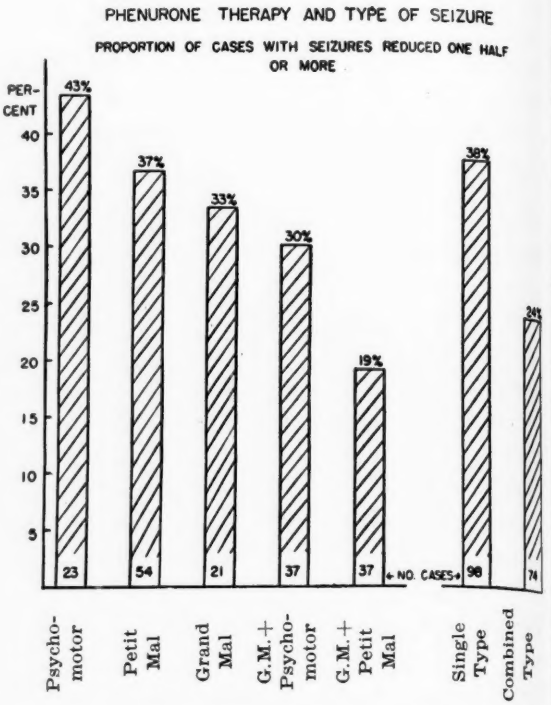

Figure 2. The proportion of patients whose attacks were reduced by one-half or more while on phenacetylurea medication with respect to the type of seizure. Percentages appear at the top and the numbers in each group at the bottom of columns. The next to the last column is the average of the first three; the last column is the average of the fourth and fifth.

the patient was subject to two seizure patterns in place of one. Thus, of 98 patients having a single form of attack, 38 percent were greatly benefited, against only 24 percent in the group of 74 patients having two forms. In the total 172 cases having seizures classifiable as one of the three common patterns, 32 percent had 50 percent or more improvement. This is greater than the 25 percent shown in Figure 1 because Figure 2 includes 10 patients who experienced excellent results, but had to stop the medicine because of side effects.

Clinical benefits are most dramatic when presented not as statistics but as case histories. Too often initial success, especially in very severe cases, is not maintained. For example, a female of 18 years with a long history of both convulsions and myoclonus epilepsy, and for the most part confined to bed, on a combination of 3.5 gm. of phenacetylurea and 0.6 gm. of tridione had for eight months been sufficiently improved to

be up and attend dances and other social events. Then intrusion of paranoic ideas required discontinuance of the phenacetylurea, although the girl's brain pathology may have played a role in her illusions.

Results can be viewed with more confidence when the electroencephalogram is improved as well as the seizures.

Patient W. H. began to have convulsions when three years old. When first seen, in May 1947 at the age of eight, he was having episodes of screaming with rigidity of the arms and clinching of the fists intermittently throughout the day every four or five days. Since the onset of attacks, he has been seriously deteriorated mentally. Treatment by ketogenic diet, phenobarbital, dilantin, bromides, tridione, and mesantoin had all failed to check the attacks. On August 12, 1948, he was dull, drowsy, ataxic and drooling constantly. He responded verbally, if at all, by grunting. On October 20, 1948, phenacetylurea 1.5 gm. was added to the phenobarbital, tridione and mesantoin he was then taking. Improvement was gratifying. He had a series of convulsions when without phenurone for five days, although he continued to take the same amount of supplementary medicines. Four months after the start of treatment, the mother wrote —"It is surprising how much more alert he is now compared to even last Fall." Two months later he was still having only mild tonic seizures, 10 to 20 seconds in duration, in his sleep. He was alert, cheerful, cooperative, talking and not drooling, though still retarded mentally. Present daily medication is phenacetylurea, 1.5 gm.; mesantoin, 0.3 gm.; and tridione, 0.3 gm. Figure 3 illustrates representative portions of three of his electroencephalograms. The first made at the time of his first visit in 1947 and the second made 16 months later and two months before starting phenacetylurea were almost continuously grossly abnormal with high voltage three to four per second waves with occasional sharp spikes or slow spike wave formations. The third record, made six months after starting phenurone, is normal for his age. The electroencephalographic tracings of another of these patients who displayed similar surprising improvement, both clinically and electrically, is in an article by Lennox and Davis.[4]

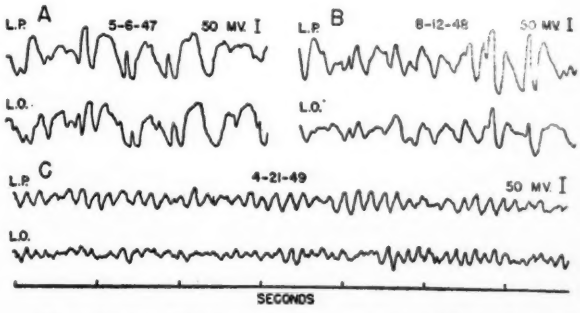

Figure 3. Short samples of the eight channel electroencephalographic records of patient W. H. Sections are from the left parietal and left occipital leads. The signal at the right marks microvolts, the line at the bottom, one second of time. Placement of electrodes was scalp to ear. Recordings A and B were made respectively in May 1947 and in August 1948, before phenacetylurea was added to the previous medication of phenobarbital, mesantoin and tridione. Recording C was made in April 1949, after phenacetylurea had been used for six months, during which time the boy was almost free of seizures. A and B are grossly abnormal with almost continuous high voltage, two to four per second waves in all leads. B is the worse, with many high voltage slow spike-wave (petit mal variant) patterns. C is normal, except for occasional series of six per second waves in parietal leads, as in the sample.

Side Effects

The good effects of medication have to be balanced against their ill effects. In approximately half the patients who took phenacetylurea, no change was noted either in their general state of health or in their emotional reactions. In remaining half, a wide variety of side effects appeared. Most reactions have been minor and not infrequently have been beneficial rather than objectionable. Even when unpleasant, reduction of dosage permitted many patients to continue treatment. The following tabulation gives the list of symptoms and the number of patients reporting each. Because a single patient may have complained of two or more side effects, the number of patients affected is considerably lower than the total of the figures noted below.

Nervous System

More active and alert, behavior improved	26
More irritable, jittery, fatigued, depressed, behavior more difficult	26
Disturbance of sleep	12
Headache, dizziness, ataxia	4
Marked depression and confusion	5
Hypomania	1
Paresthesias	1

Gastro-intestinal

Anorexia—weight loss usually slight	12
Indigestion	2
Vomiting	1
Erosions of oral mucous membrane	1
Hepatitis—Fatal	1

Skin

Rash (6 adults)	14
Urticaria	1
Angioneurotic edema	1

Blood

Neutropenia	1
Eosinophilia	1

Nervous System. By far the commonest side effects, regardless of seizure control, have been symptoms involving the nervous system, expressed as alterations in behavior or personality. Such alterations might be either pleasant or unpleasant. Which patients would react, and in what manner, proved to be unpredictable. The increased alertness, improved effectiveness, and better behavior—symptoms mentioned specifically in 6 patients, might in some cases be attributed to the improved seizure control. The opposite group of symptoms (irritability, "jitteryness," fatigue, depression or difficult behavior) present in 26 patients accounted in the children for nearly half of all their list of undesirable reactions. In both children and adults sleep disturbances included bad dreams, restlessness, delay in falling asleep or early arising with sound sleep intervening.

In the series of Gibbs et al[2] 20 percent of the patients showed unpleasant personality or psychic manifestations often alarming in their intensity. Some of Zeifert's[3] veteran patients were similarly affected. In contrast, only five of the 178 patients displayed pronounced symptoms (depression and confusion or extreme excitability) and only one of these was a child. Cause for the decreased incidence of severe emotional or psychic reaction to this drug in children as compared with adults warrants further study.

The difficulty of evaluating the side effects of medication in patients with pre-existing personality disturbances is illustrated by the case of J. M., a 36 year old, unmarried commercial artist, subject to psychomotor seizures uncontrolled by medication over a 14 year period. For at least seven years, he had been subject to periods of depression. Because of two suicidal attempts the year before, he had been committed to a mental hospital. He was placed on phenacetylurea, 2 to 3 gm. a day, and for 13 months there was rarely a detectable seizure. After five months he again became depressed and was readmitted to the hospital where the phenacetylurea was continued in customary dosage. He regained his weight and spirits and in five months was discharged to resume his work. Three months later he again became depressed. However, in an interview with one of us he expressed pleasure and satisfaction because of his continued freedom from attacks. Nevertheless, three weeks later he ended his life by drowning. Whether the medicine was a contributing factor in his death is an open question.

A history of periods of abnormal or violent behavior does not necessarily mean that the drug will increase the difficulty. The case that follows illustrates a remarkable improvement both in seizures and in psychic disorders.

J. S., a boy of 17, was first seen in 1946. He had had petit mal at a frequency of 20 to 30 a day for four years and grand mal for three. The latter recurred about five times a month. For two years he had been quarrelsome and opinionated and had lost interest in school work. His electroencephalogram disclosed numerous bursts of three per second spike-wave complexes, characteristic of petit mal. He was given a combination of dilantin, mebaral and tridione, and later dilantin, mesantoin and tridione. The clinical petit mal were eliminated, the convulsive seizures were absent for three months, then gradually returned to a frequency of one every three weeks. On July 24, 1948, the boy went into status for 24 hours, became disoriented and aggressive; and, for this reason, was admitted to the New Hampshire State Hospital, where in a week the psychosis gradually cleared and he returned home. A month later the outburst of convulsions and psychosis followed by commitment was repeated. Three weeks later, without preceding seizure, he suddenly became mentally disturbed and violent and continued in this condition for a week. "Wherever

the door to his room was opened, he ran about the ward trying to kick and hit everyone. He continually pounded on the door and broke windows. He had to be given sodium luminal injections in large dosage as he refused to take anything by mouth." Following this episode, on September 28, 1948, the patient was given phenurone without other medication. The dose was gradually increased to 2 gm. a day. Nine days after starting the drug, he became garrulous, confused, could not sleep at night. He wrote in a letter, "my name isn't J. S., it's Jesus Christ." Two days later he had two convulsions lasting 10 minutes, but without psychosis following. The following month there were two more convulsions, but again without psychosis and he was discharged from the hospital on December 6, 1948, on a dose of 2.0 gm. of phenurone a day. Three single grand mal recurred at 30 day intervals, but no further psychotic episodes. In March 1949 the phenacetylurea was increased to 3 gm. daily (without other medication) and for the past nine months the patient has been seizure free, as well as free from abnormal behavior or side effects of medication.

The argument might be advanced that the outbursts of violence and the periods of confusion or the illusions were themselves epileptic seizures, but whatever their nature the drug exerted a soothing rather than an exciting influence.

Gastro - Intestinal Symptoms. Loss of weight observed in 10 cases was usually attributable to mild anorexia, possibly secondary to fatigue and irritability, although in three patients the appetite was unimpaired. These patients, although in excellent health and spirits stimulated by the drug, were "burning the candle at both ends" and losing sleep. Indigestion was observed in three cases, one of whom had vomiting. Weight loss was the main reason for stopping medication in four patients.

Although toxic effect on the liver was noted in only one case, this ended in death. One or two other deaths in which the drug may have been implicated have occurred[5] and liver tests carried out routinely have shown a disconcerting proportion of patients with positive tests for urobilinogen. Doubts on this score have so far interfered with the placing of the drug on the market.

The patient, M. M., a man aged 36, had had occasional convulsions and severe daily myoclonic jerks for 28 years. The jerking was most severe on dozing. As a consequence, an hour or more would be consumed in getting to sleep since the jerking would wake him out of his doze. However, dilantin controlled convulsions and paradione in a dosage of 1.8 gm. held the jerks in check. In an effort to bring further relief, phenacetylurea, 2.5 gm., was added to the other medication. The initial results were pleasing with reduction in jerking and increase in alertness. After three weeks, there began lethargy, diarrhea, anorexia and indigestion. Symptoms were at first attributed to an epidemic gastro-intestinal disturbance then prevalent in the community. Physical examination was normal. Two weeks later phenacetylurea was reduced by 0.5 gm. and after another week was stopped entirely, six weeks after it was started. The next day jaundice was noted and the patient was admitted to the Massachusetts Memorial Hospital where he died five weeks later. Autopsy findings revealed acute, severe, parenchymal damage to the liver, superimposed on an older portal cirrhosis of mild to moderate degree. Only an outline of the case is given here, since the complete findings will be published elsewhere by the pathologist of the hospital, Dr. Rudolph Osgood.

Skin Reactions necessitating discontinuance of medication occurred in 15 patients an undue portion of whom were adults. Appearing seven to 25 days (average nine to ten days) after initiation of treatment, the reaction usually began with flushing of the face and neck, a sensation of warmth, often a headache and a degree or two of fever. Within an hour, the neck and trunk became speckled with an erythematous maculopapular, slightly pruritic rash. In severe cases this would spread to involve the extremities. The eyes might become bloodshot and in one case there were erosions of the oral mucous membranes. Fading of the eruption occurred within 4 to 48 hours after discontinuing medication. Frank urticaria

and angioneurotic edema each occurred in one patient.

In three patients, an eruption of a pustular type, acneform in character and distribution, developed after prodromal symptoms similar to those that preceded the morbilliform rash. The acneform eruption seemed less explosive, but subsided more slowly. Two of the three patients were able to resume medication in reduced dosage despite a continuing low-grade eruption.

Blood. The total white blood count remained constant or else rose only moderately in response to a skin reaction. Occasionally a rise in the proportion of eosinophiles accompanied the leukocytosis. In one patient of 10 years with an allergic background, the percentage of eosinophiles at the height of the reaction reached 58 percent. In another six year old child the neutrophiles fell from a premedication count of 5300 to 1000 and the child had also a generalized rash.

Discussion

A new anti-epileptic today faces the hurdle that it must either be more effective or have fewer side effects than those now in use. Giving a drug only to those patients who have failed to respond to vigorous therapy with standard drugs imposes a severe test and any demonstration of effectiveness is hailed with enthusiasm by patient and doctor. In our series, as in the smaller ones already reported, approximately one-half of the members were better when phenacetylurea was either substituted for other medicines or was added to them. Failure of continued improvement, or appearance of toxic symptoms may reduce the number of those semi-permanently improved to only 20 to 25 percent of the total. But this group includes many with the resistant psychic or psychomotor type of seizure. As with other anti-seizure remedies, results are best when the drug has but one seizure pattern to contend with. Phenacetylurea can dramatically improve the immediate outlook of a small proportion of patients treated.

The possible toxic effects somewhat modify enthusiasm. For this reason, patients taking this medicine must be closely supervised. The patient or his family must be told what to look for, and should be able to report unusual nervous symptoms or changes in mood, skin rashes or gastro-intestinal upsets. Although unequivocal instances of aplastic anemia have not been reported, periodic, probably monthly, examination of the blood is an essential precaution. More disturbing, because less easily guarded against, is possible hepatitis. In our own fatal case, there was pathological evidence of a pre-existing liver injury which probably accentuated the toxic action of the drug. Therefore, this treatment should be withheld from patients with a history of jaundice or use of toxic agents such as large amounts of alcohol. Symptoms of early liver toxicity are vague and not distinguishable from the nervous reactions of fatigue, depression or anorexia and indigestion. Zeifert[3] has reported alterations in a number of liver function tests given to 13 cases taking phenacetylurea for six months. Two of our adult patients who complained of indigestion, anorexia and tiredness reacted normally to a battery of such tests. A number of cases, as yet unreported, of liver dysfunction or damage (two with death) have come to our attention. Whether periodic chemical examinations of the urine and blood for evidence of liver toxicity can prevent the severe degrees of liver damage, must be determined. We have initiated such a study. The liver has many functions and a battery of tests is preferable to one test such as the quantitative estimation of urobilinogen in the urine. Obviously the toxic effects differ widely in the experience of different observers. A compound that preserves the therapeutic but eliminates the toxic effects of phenacetylurea would of course be ideal.

Pediatricians may have some assurance because so far children have not been subject to the severe psychic or gastro-intestinal symptoms reported for adults.

Summary

A new anti-epileptic drug, phenacetylurea, not yet on the market, has been given to 178 epileptics, three-fourths of them children, whose seizures had not been controlled by other drugs. It was usually given as a supplement to existing medication. Improve-

ment was noted in approximately one-half of the patients treated, this persisting for periods up to 14 months. Approximately one-fourth had at least a 50 percent reduction in attacks. The percentage of patients improved to this extent (including those who had to stop medication because of toxic symptoms) varied with the seizure pattern; namely 43 percent when there were psychomotor seizures only; 37 percent for petit mal only; 33 percent for convulsions only. When there was a single type of seizure the proportion improved (38 percent), was greater than when a combination of types existed (24 percent). The relative success with psychic (psychomotor) epilepsy is especially welcomed. The drug can be a valuable adjunct to treatment when other means failed.

The frequency of a variety of side reactions—nervous, gastro-intestinal, cutaneous, and hematopoetic—makes careful supervision mandatory. The largest fly in the ointment is evidence of dysfunction or damage of the liver in certain adult patients. Our series included one death from hepatitis. The drug should be withheld if there is suspicion of previous liver damage and if periodic examinations of liver function cannot be carried out.

Author's Note: The supplies of phenurone used in this study were furnished by Abbott Laboratories, Inc., North Chicago, Illinois.

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Biological Interpretation of the Basic Factors Governing Behavior

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Ever since organized society has existed it has demanded of its members conformance to certain established modes of conduct. Some rules were established by society for the protection of its members; others grew out of the customs, usages, philosophies and varied sentiments of the community. To secure observance of accepted modes of conduct has long been the problem of governmental agencies, the schools, the churches and more recently of social betterment groups. This problem has recently been receiving greater attention because of the difficulties with adolescent youth in unacceptable conduct termed delinquency.

The views expressed in this article are based on the writer's own study, observation and experience. Direct quotation from any particular author has, therefore, been omitted. Material pertaining to common knowledge on the subject was obtained from many sources. "Psychology Normal and Abnormal" by James Winfred Bridges has been the writer's guide in his studies for many years.

In view of the scientific nature of this article certain terms must be defined in order that a word may universally convey the same idea. Webster's International Dictionary, 1934 edition, is the authority used for the definitions presented. Many of the definitions were recast to make for smoother diction but the original meaning is retained.

Science is thus defined as the accumulated and accepted knowledge, systematized and formulated with reference to the discovery of general truths or the operation of laws relating to the phenomena of the universe.

Psychology is the science which treats of

the phenomena of consciousness and behavior. It is the study of an organism as an individual unit and its activity in relation to its physical and social environment. It is basically the study of the response of living things to the stimuli of the environment.

The definition for mind presented here is a composite and abbreviated form of several conceived by various groups of psychologists. Mind is the agent in thinking, feeling or performing any action. It comprises the conscious states of the individual and his adaptive ability. More explicitly stated it is that something by which an organism becomes aware of an adjusts itself to environment.

Consciousness is an intangible thing which has never been clearly defined. The word is synonymous with awareness and also with mind. Our own consciousness makes itself evident and understandable.

The conduct of an individual is his behavior. Behavior is defined as the individual's activity as eventuating either visibly in muscular movement and invisibly in glandular secretion.

Biology is that branch of science which treats of living organisms. The common characteristics of all living things is birth, growth, reproduction and eventual disintegration. Living things are separated into two classes, vegetable and animal. The former obtains its nutrition largely, if not altogether, from the inorganic matter in which it is stationed. The latter must obtain other organic matter as the nutrient material for its sustenance. It must then have some sort of a motor apparatus to contact such material.

A substance found in the structure of all living things is protoplasm. This is considered to be the basis of all life. Its properties, metabolism, growth, reproduction, irritation, conduction and contradiction are manifested in some degree in all living things. Because animal life is dependent on some form of movement to secure nutrition the latter three properties have reached a greater degree of development in this form of life.

Living things appear in various forms which again have various degrees of complexity of structure. The greater the complexity of structure the greater is the division of labor among the cells. Special tissues are found for the function of irritation, conduction and contraction. These structures constitute the sensorimotor system of the more complex organisms. This integrated system is recognized as the organ for consciousness and behavior.

The principle of the sensorimotor system is response to stimulus. The structures for this mechanism are various: sense organs, efferent nerve tracts, internuncial nerve tracts, afferent nerve tracts, muscles and glands.

The physiologicol correlates to these structures are: 1) A stimulus acting on a sense organ initiating a nerve impulse; 2) Conduction of the nerve impulse over an afferent sensory nerve tract to the central internuncial tracts; 3) Integration of the nerve impulse in the central tracts for orderly response; 4) Conduction of the integrated nerve impulse over an efferent motor tract to a muscle or gland; 5) Coordinated action of a muscle or a glandular secretion.

There are various levels at which a nerve impulse may be transferred from the afferent nerve tracts over the internuncial tracts to the efferent tracts. A transfer occurring at one of the lower levels ends in a response of which the organism is unaware and is called reflex. By this type of response the vital functions of the body as circulation, digestion and the intricate muscular coordination is carried on. A transfer occurring at one of the higher or cerebral levels ends in a response of which the organism is aware. By this type of response the so-called voluntary or conscious activity is carried on or inhibited. It is only when this type of cerebral activity is in progress that consciousness is observed or experienced.

Of the prevailing theories regarding the mind-body relationship the double aspect theory is probably the most comprehensible. It holds that neural activity and consciousness are the objective and subjective aspect of the same thing. Neural activity is the thing observable and consciousness the thing experienced. It neither affirms nor denies that consciousness is purely a mani-

festation of neural activity nor that it may or may not be a metaphysical phenomenon.

Psychology recognizes three major aspects of consciousness. These are cognition, affection and conation or knowing, feeling and doing. The neural correlates for cognition and conation are quite well established in the sensory and motor areas of the cerebrospinal nervous system. The neural correlate for affection has not been so definitely established. The autonomic neuroglandular system through its connection with the cerebrospinal system is quite generally accepted as that correlate.

Constitution is the structure of the individual's physical body plus the nature of each aggregate part as manifested by the physical and vital power expressed in its function. The nature of one's body limits the scope of his activity and the degree of its efficiency. One's constitution is innately determined.

Another innately determined factor in behavior is instinct. It is defined as a tendency to action which leads to the attainment of some goal natural to the species not dependent on previous experience. Instinct is probably the most readily understood if viewed as being based on the psychological principal that all movements originate from the stimulation of a sense organ. Sustained stimulation of a sense organ produces a state of neural excitement. This excitement produces the urges and drives which constitute the subjective aspect of instinct. To secure relief from this excitement random movements occur but because of neural patterns innately determined apparently in the nature of the synapses a response occurs sufficiently orderly to relieve this excitement. By securing relief from neural excitement the preservation of the individual and species is accomplished. Sustained stimulation of any sense organ produces the neural excitement particular to that sense organ. A definite sense organ for each form of neural excitement has not been demonstrated. Some structures have been demonstrated in the skin as the sense organs for pain, temperature and pressure. A sense organ for either the sensation of hunger, thirst or lust has not been identified but plausible theories have been advanced as to their nature. The instinctive response to neural excitement is soon modified by learning but the urges and drives are never in abeyance, and tend to insure the perpetuity of the species. The instinctive drives cannot be suppressed but may be deflected into channels leading to socially acceptable behavior.

Learning is an acquisition by an organism of knowledge, skill or mode of behavior. Neurologically it is the formation of new neural connections according to the law of association. This law states that if two or more neural systems are active at the same time the resistance of the synapses between the systems is lowered so that later activity in one system may spread to the other.

Habit is defined as a settled tendency to a certain manner, custom or practice of procedure. Habit is an acquired mode of response. Habitual movements constitute the greater part of human activity. One's habits are largely acquired by imitating the conduct of those about him. One's routine adjustment to his environment is habitual. Frequent repetition of a movement causes it to become automatic but may reappear in consciousness. One's mode of living is largely habitual.

Ennui is defined as a feeling of weariness and dissatisfaction; languor of spirits, tedium, boredom. Activity to secure relief from ennui is a large factor in behavior. Recreational and amusement projects may exist as means of securing sensuous gratification but more likely as means for relief of boredom. The multiplicity of theatres, night clubs, beer gardens, athletic arenas and gambling dens is significant of something more than the desire for pleasure. The most striking thing common to all people is that people are always going somewhere. The procurement of a livelihood requires some movement but the greater stimuli seems to be the relief from boredom.

To play is to engage in a sport or lively recreation or to amuse or divert oneself. Play is so extensive that it must have purpose. One obvious purpose is the relief of ennui. Another rather significant purpose seems to be to train the sensorimotor system to react to a controlled situation so that

later it may react in orderly fashion to a strange situation.

The mechanism of sleep is still largely speculative. It serves the purpose of securing rest for the body. It is definitely a means for relieving boredom. It is the infant's only relief from boredom until he learns to play.

Culture is the complex of distinctive attainments, beliefs, traditions, etc., constituting the background of a racial, religious or social group. The culture of a people determines to a large extent the nature of the environmental influence on the individual. From the cultural background of a people their habits, sentiments and beliefs are largely derived. Such culture has a profound effect on the behavior of the individual. To the extent to which he accepts this culture is he socialized.

A sentiment is a mental attitude, conception, idea or belief intermingled with feeling arising out of the individual's experience with reference to some object or class of objects. A belief is a mental endorsement or acceptance of something thought of as real. A belief readily acquires a feeling tone and becomes a sentiment. This applies particularly to one's political and religious conviction. A sentiment having an idea of feeling tone also has a tendency to action. One's principles, prejudices, ideals, interests, aversions, aims, purposes, etc. are sentiments. The sentiments one acquires largely charts his course through life.

Reason as it concerns behavior is defined as a consideration, motive or judgment, that influences the will or leads to an action or a course of action. As such, reasoning is a factor in planned behavior.

Instinct is the force that initiates behavior, constitution determines its scope, habit shapes its mode and sentiment directs its course. Reason becomes a factor in behavior in perplexing situations especially when the security of the individual is threatened.

Ego is defined as the self whether considered as an organization or system of mental states or as the consciousness of the individual's distinction from other selves. A thing is whatsoever is thought of as having separate entity. An organism is a thing. The ego is an organism's consciousness of his distinction from other things. This consciousness results from neural stimulation. Anything that alters the state of the nervous system affects the ego.

Personality (psychol) is defined as a) the totality of an individual's characteristics, especially as they concern other people; b) an integrated group of emotional trends, interests, behavior tendencies, etc. The writer likes to think of personality as the ego and all its attributes. These attributes are manifested in his personal appearance, manner of speech, movements, instinctive drives, intellectual development, emotional reactions, etc.

Happiness is defined as a state of well-being characterized by relative permanence, agreeable feeling and by natural desire for its continuation. This condition requires a state of harmonious relation among the attributes of the ego, especially between the sentiments and the instinctive drives. It is essential to happiness that the latter have reached a state of maximum satisfaction and the organism attain a sense of security.

Conflict (psychol.) is defined as the presence of opposing desires or tendencies. Living things in general are free to follow their instinctive drives but this is not so with the human unit. He must be governed by social conventions which interfere with direct ways of securing relief from these drives. An adjustment must be made between the instinctive drives and the sentiment of social esteem or conflict results. An unsolved conflicts leads to the lowering of self esteem.

The three major aspects of consciousness knowing, feeling and doing are all active in organizing the response to the stimuli from the environment. The feeling element is probably the most vital in bringing about the welfare of the organism because it incites the urge to live and the urge to mate. These urges bring about the organism's preservation and perpetuation. To secure the realization of these instinctive drives the organism finds itself in competition with other organisms and creates in man the desire for omnipotence or mastery over the environ-

ment. The degree to which this desire is realized determines the sense of superiority of the ego and the degree of failure its sense of inferiority.

An emotion is defined as a departure from the usual calm state of the organism; it includes a distinctive feeling tone, an impulse to overt action and a characteristic trend of activity of the body mechanisms particularly of the autonomic muscular and glandular system. Any of the states designated as fear, anger, disgust, grief, joy, surprise, yearning, etc., is an emotion. Everything in nature has its purpose. The strong feeling element in an emotion appears to have the purpose of enforcing the instinctive drives in situations that demand an intense response. It is a psychological principle that emotional activity occurs in response to a situation actually experienced or ideally represented and does not originate spontaneously. The nature of each one's neuroglandular system determines to some extent the intensity of the emotional reaction. Because of having a neural element there may be a habit element in the emotional reaction expressed in behavior.

Memory is defined as the process by which a previous experience is ideally reproduced in consciousness and recognized in its time and order. It is through memory that an individual's present identity is associated with his past identity. Every experience of an individual is thought to leave its trace in the nervous system in the form of a neurogram. By the process of association the neurogram may be reactivated in consciousness. Every present sense experience must be associated with the memory of a past experience in order to have meaning.

Inhibition is a restraint upon one psychical activity by another. An organism's sense organs are constantly bombarded with stimuli. The resulting nerve impulses must be integrated into an active or inhibited response. If the impulse to action is associated with a pleasant previous experience action is apt to occur. If the impulse is associated with an unpleasant one inhibition is apt to take place. Feeling is the determining factor. It is the principle of punishment and training to associate an unpleasant experience with the commitment of an undesirable act, and to associate a pleasant experience with the performance of one of a desirable nature.

Conscience is the sense or consciousness of moral goodness or blameworthiness of one's conduct, intentions or character with a feeling of obligation to do or be that which is recognized as good. This is a descriptive definition. Conscience is manifested in the form of a sentiment, that of goodness and of badness. These sentiments have a strong feeling content. Conduct in accord with the sentiment of goodness incites pleasurable feeling, likewise conduct in accord with the sentiment badness incites the opposite feeling. Conduct in accordance with the sentiments of goodness gains social esteem and in the metaphysical sense the approbation of the deity. This adds to the sense of security of the individual and lessens his sense of inferiority. Conduct in accord with the sentiment of badness has the opposite effect and accentuates the individual's sense of inferiority. Feelings of guilt or remorse are the individual's own sentiment of failure to attain his pretentions of goodness. The feeling tone accompanying the idea of failure is the distressing element.

Discussion

The human organism at birth is obviously devoid of experience and, therefore, devoid of knowledge. His power of movement is very limited but he is not devoid of feeling. His first movements are reflexive and instinctive through neural pathways that were innately formed. The instinctive movements are manifested in breathing, suckling and crying. These bring him the assistance he needs to ease his discomforts.

As the infant organism matures he develops a personality. His constitution and instincts have been innately determined. His constitution at once determines in what habitat he can survive, the type of nutriment he must secure and what means of locomotion are at his disposal. It determines the power and speed of his movements, the mentality he may develop, and in fact, all his vital forces and powers.

The instinct to survive is the greatest force producing activity. It is the drive that compels him to seek sustenance, shelter and safety, totalling security. He soon learns he must do this in a manner prescribed by society. With the maturation of the reproductive organs the mating urge appears. He has already found the prohibitions set up by society against procuring the necessities for his existence quite high. He finds the social barriers against the relief of the mating urge almost insurmountable. Society is governed by its cultural traditions. To have social esteem he finds he must observe social traditions.

The innate components of the personality are inalterable. The habits and the sentiments of the personality are acquired from environmental influences and are accidental but alterable. The child acquires his habits from his association and modifies them as his environment changes. With experience comes knowledge and with knowledge ideas. Ideas acquire feeling tone and sentiments are formed. A child soon forms his likes and dislikes. From his early infancy he is exposed to the sentiments of his family. Later the school, the church, the press and other agencies are all active to indoctrinate him with their tenets.

These are the factors that determine behavior. The instincts are innate in all living things, and the driving force of behavior. This must be recognized in the evaluation of an individual's conduct. Habits take care of his routine daily activity but may change if there is an incentive. The sentiments control the direction of his behavior either because of the feeling element or because of the ideational content.

The cultural background of a social order shapes the standard of conduct it demands of its members. Governmental agencies are established to bring about conformance to these standards. Innumerable agencies are active to indoctrinate each individual with the tenets it represents. These tenets may be conflicting and not all for the best interest of society or the individual.

Society could give more recognition to the importance of directing the instinctive drives of its members. These must be deflected into acceptable channels for the welfare of the social order if it is to retain its existent status quo. The individual's habits are amenable to change with environmental conditions. His sentiments are largely the result of indoctrination but are changed by experience. It should be realized that feeling is as great a factor in directing conduct as reason.

Summary

The intent of this article is to present in a scientific way the basic factors that govern the behavior of all living, moving things.

The study is presented from a biological point of view and embodies the psychological principle that all movement is the ultimate result of a sensory stimulus.

The nervous system is considered to be the organ for consciousness and behavior. The double aspect theory regarding the mind-body relationship is advanced.

The innate factors in the determination of behavior are the individual's instincts and constitution.

The instinctive factors are presented as based on the principle of response to stimulation involving neural excitement.

Ennui and play are presented as factors of importance in the study of behavior.

Habits and sentiments are the alterable factors in behavior and are largely derived from the cultural background of the individual.

The ego is considered to be the consciousness of a self as distinct from other things and on a neural basis.

The ego is presented as the center about which the personality is formed. It is the part of the organism that causes it to strive for omnipotence and mastery over the environment. It finds happiness when its attributes form a harmonious relationship.

The cultural background of a social order is considered to determine the standard of conduct demanded of its individual members. To be socially acceptable a person must not deflect his course of conduct too far away from this standard.

Use of Tolserol (Myanesin) in Hyperkinetic Disorders

(with Special Reference to Postencephalitic Parkinsonism)

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Many different types of treatment have been advanced during the past 130 years since James Parkinson first described the syndrome bearing his name.[1] In spite of the introduction of many new therapies, both medical and surgical, the most efficacious so far has been the solanaceous alkaloids which have some effect in reducing the rigidity without materially lessening the tremor unless given in amounts sufficient to cause autonomic side-effects such as inaccommodation, asalivation.[2]

The ability of the alpha substituted glycerol ethers to produce muscular relaxation and even paralysis was first reported in 1946 by Berger and Bradley.[3] The most potent was found to be 3-ortho-toloxy-1, 2-propanediol, Tolserol, in which the alpha substitution is an ortho-tolyl group.

During the past two years Stephen and Chandy,[4] Schlesinger et al,[5] and Hunter and Waterfall[6] have suggested Tolserol as being useful in extrapyramidal syndromes and recently its effects upon the central nervous system were reported by Gammon and Churchill.[7] Berger and Schwartz[8] found reduction of tremor and rigidity after its administration; however, some of their patients derived less benefit than others and they postulated this due to one of three things: too low dosage, incomplete absorption or insensitivity. Their route of administration was oral, the elixir preparation was used, and their results were best when combined with the drugs of the atropine class.

A Tolserol analogue Lissidiol** having a very low water solubility has been used. In dogs, oral doses of 150 mg. per kilo. produced an ataxia comparable to that obtained with 625 mg. of Tolserol. This ataxia is produced in a slightly shorter time and lasts nearly twice as long. The state of depression or paralysis obtained upon intravenous or oral administration in animals, blood pressure effects and the action upon respiration and cardiac function are very similar to that obtained with Tolserol. The chronic toxicity test in rats parallel those with Tolserol using the same dosage. Lissidiol has approximately the same activity as Tolserol intravenously in dogs but more than four times the activity orally with a little more than twice the duration. This analogue is effective in most cases and it seems entirely possible that Lissidiol may be more effective in Parkinson's syndrome. This possibility is being investigated.

Method

Eighteen patients with postencephalitic Parkinsonism comprise the bulk of this study. After six months of supervised administration it can be stated with reasonable certainty, that Tolserol is efficacious when combined with the solanaceous drugs in reducing the tremor and rigidity, and that it partially effects the hypervigility. These effects are transitory (fifteen minutes to five hours) as shown in table 1.

Control studies were done with intermittent placebo substitution. Oral, rectal and vaginal administration was used depending on the cooperation of the patient. Oral tablets and/or elixir were preparations of choice and patients were given a certain amount of freedom in juggling their dosage, but the daily dosage never exceeded five grams in divided doses. No attempt was made to upset established solanaceous regimes but rather to supplement them. Suppositories were made to contain one gram of the powder; cocoa butter was used as base, and they were inserted rectally and/or vaginally.

*From the Department of Neurology, Graduate Hospital of the University of Pennsylvania. Read before the Philadelphia Neurological Society, College of Physicians, Philadelphia, April 22, 1949.

**Trade name, E. R. Squibb & Sons.

TABLE 1

Estimated Therapeutic Value
(Relative)

Administration	Onset	Therapeutic Effect
Oral, one gram:		
Tablet	10—30 minutes	20—40 minutes
Elixir	5—10 minutes	15—30 minutes
Capsule	15—30 minutes	15—40 minutes
Suppositories, one gram:		
Vaginal	Gradual 15 minutes	1—1½ hours
Rectal	Gradual 15 minutes	1—4 hours
Intravenous, 2% solution, 150 cubic centimeters:		
Parkinsonian	2—3 minutes	2—5 hours
Spinal syndromes	4—6 minutes	2—12 hours

Twenty-six cases were studied. Eighteen with postencephalitic parkinsonism and eight with miscellaneous neuromuscular disorders. Of the eighteen cases of parkinsonism all responded to intravenous administration and all received some effect, however transitory, from the elixir. The relief of tremor and/or rigidity was about equal in all cases, perhaps somewhat in favor of tremor. In two of three cases the frequency of oculogyric crises was diminished, however Tolserol has no effect when given during a crisis. Two cases had no atropine derivatives and improved, and two did not respond favorably; both of the cases were far advanced, addicted to hyocine, and were uncooperative. They must be considered failures. One case in which the tongue protruded rhythmically responded well. Patients were able to sew, write, shine shoes, type, and sweep easier while under the effect of the drugs. No effect was noted upon speech or salivation. The drug was also administered in miscellaneous neuromuscular disorders as follows:

Encephalomyelopathy of unknown origin. Duration about two years. Numbness and weakness of the right hand of six months duration, and inability to write legibly for four months. After administration of one gram the patient was able to write legibly for about twenty minutes and then reverted back to the previous tremor.

Westphal's pseudosclerosis of five years' duration. Developed marked tremor of the head and upper limbs. Was given one gram four times daily. The patient wrote the following note, "It was almost impossible to find someone to pull me up to a sitting position. When I was assisted, I was able to control my neck muscles sufficiently to hold my head up straight . . . after this the head tremor started again and I had pains in the head, neck and back. Again after taking the tablets the tremor and pain stopped. I cannot state whether the drug has helped me or not but for the time after taking it I have improved in control of my limbs."

Familial tremor of three years' duration limited to both hands. Father, eighty-five, has same tremor, of fifteen years' duration. Patient was given one gram in divided doses supplemented with one-quarter gram of elixir between tablets. The tremor almost disappeared, this effect was longer than with other tremors I have had experience, and it was not easily produced before an audience. This tremor returned with each placebo substitution. Lissidiol was used with success in this case.

Amyotrophic syndrome of two years' duration with bilateral frozen shoulders due to two cervical discs demonstrated by myelography. This patient was given the 2% solution intravenously and had marked improvement of shoulder motion which lasted about 12 hours when the pain and rigidity returned. The drug was helpful in myelography in this case.

Convulsive status. Jacksonian fits of the right side of the body every minute. Intravenous preparation did not decrease the number of seizures but reduced the intensity considerably so that the right leg remained motionless, the right arm was less rigid, but the head and eyes still deviated to the right. This effect lasted about two hours. This patient had a parasaggital astrocytoma verified by operation.

Two severe low back syndromes of eight months' duration or more. These were mechanical backs with negative myelographic studies. The drug afforded no relief of pain and reduced muscle spasm only slightly. This pointed to nerve root compression. At operation both cases showed a herniated nucleus pulposus with severe root compression.

Bilateral bursitis with frozen shoulders. The intravenous 2% solution was given with relief of symptoms and a return to normal shoulder motion range. This patient has been well since.

These cases illustrate the action of Tolserol. Better plasma levels were obtained when the drug was administered in the elixir as compared with the tablet form. This is probably due to superior absorption. Negative results may be due to use of the tablet form only. Effron's patients[9] did not have a good clinical response, but they were much more advanced in their disease than mine. They were older and not all postencephalitic. Many, if not all, were arteriosclerotic, which is probably a factor when one considers cerebral blood flow reduction as postulated by Shenkin and Groff.[10] Nausea and vomiting accompanied by vertigo is probably due to overdosage. This is not present in all cases especially those in which there is little effect; or those with poor adsorption

from the intestinal mucosae. The intravenous administration is particularly favorable when used before myelography to relieve muscle spasm when it becomes necesary to stand the patient upright to move the column of pantopaque cephalad. Results were encouraging in familial tremor, status epilepticus, frozen shoulder syndromes, and the acute low back and cervical spine syndromes. I think it reasonable to agree with Schlesinger[11] in his statement:

"In the acute low back and cervical spine syndromes, the specific relaxant and analgesic effect of Tolserol has a proper place. As an aid or substitute for traction it is most efficient. In the treatment of the acute low back and disc syndromes it seems to be of value in reducing muscle splinting and affording abrupt relief of pain. If the pain is in part due to muscular changes, relief is dramatic and may be of long duration. If the pain is secondary to severe nerve root compression, the relief is followed by an equally rapid return of pain. This response has proven of real diagnostic aid in evaluating conservative treatment of the herniation of the nucleus pulposus. Where the pain returned shortly, or was inadequately relieved, I have never seen an adequate response to conservative treatment. In such case the root is probably compressed against the incarcerated lesion and cannot be freed by muscular relaxation or skeletal traction. The saving in time and money to the patient is considerable if a long and disappointing trial on bed rest can thus be avoided."

Toxicity

In some cases Tolserol was given too frequently and the patients complained of weakness, either in the arms or legs accompanied by a feeling of lassitude. This was alleviated by reducing the daily dosage. I was unable to demonstrate any cumulative effect. Only one patient complained of nausea which was overcome by changing to the elixir preparation. I was unable to find any appreciable drop in the white blood cell counts and no evidence of leukopenia as Gammon and Churchill found in two of their eight cases. There was no evidence of hematuria nor hemoglobinuria as was reported earlier by the British investigators. No toxic effect was found to be great enough to discontinue administration over a six month period to these patients with postencephalitic parkinsonism.

Summary

Tolserol appears to be a useful adjunct when combined with the solanaceous drugs in treating postencephalitic parkinsonism, and some other hyperkinetic disorders. Under combined therapy the patient has a greater freedom of motion, and in some instances is able to again perform such tasks as shoe shining and typewriting. It is of practical value as a relaxant if given intravenously before cervical myelography. Its therapeutic effect is limited because of rapid excretion; this probably accounts for its low toxicity. More successful attempts of modification of adsorption and/or conjugation should be sought in order to obtain a longer therapeutic effect. More clinical trials will have to be made with the analogue Lissiodiol.

Author's Note: The drug, Tolserol (known abroad as Myanesin) used in this study was supplied by E. R. Squibb and Sons, New York City.

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Cervical Cord Tumor Simulating Cerebral Vascular Disease

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High cervical cord tumors are not uncommon but often present diagnostic difficulties. The present case has many unusual features, especially that of complete absence of sensory changes, absence of spinal fluid block and negative roentgenographic findings. In addition, the decision for surgical exploration was made without the use of myelography. Contrast myelography was considered inadvisable because it would have been very difficult to prevent the medium from entering the intracranial cavity due to the patient's thick rigid neck.

The case we are presenting showed essentially symptoms of motor involvement of all four extremities with spasticity and atrophy, no sensory findings except for some subjective root pain over the left chest, right shoulder and mandible, negative cervical spine x-rays and normal cerebrospinal dynamics. The motor symptoms were progressive over a period of five years until the patient was seen by one of us on January 8, 1948 at which time she was almost completely quadriplegic.

Cases have been reported in which tumors were found that appeared large enough to block the entire canal but normal dynamics were shown by lumbar puncture. Elsberg[1] states that in about 20 percent of the patients with spinal cord tumors, the Queckenstedt test may be expected to be negative. Ayer, Stookey and others[2,3] have found a smaller percentage of negative dynamics in cases with spinal cord tumor by using a refined technique of combined cistern and lumbar punctures. Stookey, Merworth and Frantz[3] have shown experimentally that there is no change in normal dynamics until the opening in the canal is definitely less in size than the opening in the puncture needle. Also, if a tumor is of such size that it nearly fills the canal the intraspinal pressure may keep an opening larger than the needle. Upon removal of fluid the intraspinal pressure decreases sufficiently to permit dura and arachnoid to come in contact with the cord and the tumor thus produces block. This will explain the reason why block may show after removal of some of the spinal fluid.

Jelsma[4] reported a series of hourglass tumors of the cervical spine in which the symptoms were the same as those of any other cord tumor with the exception that the lateral x-rays of the spine revealed an enlargement of the intervertebral foramen. In our case the x-rays of the spine revealed no significant bony change. In Jelsma's patients the intraspinal portion of the tumor was either extradural or intradural and the extraspinal part was in the paravertebral region extending through the intervertebral foramen. The tumors were found to arise from the canal membranes, nerve roots, and infrequently the ganglia. In most of the cases they were circumscribed and benign.

Craig and Sheldon[5] of the Mayo Clinic reported some interesting clinical manifestations in 91 patients with tumors of the cervical region in a series of 597 pathologically verified cases. The first symptom in 63 of the 91 cases was pain. Only 61 percent of 34 patients who had neurofibromas indicated pain as the initial symptom, whereas 71 percent of the patients with meningioma had pain as the first symptom. The lower frequency of pain associated with neurofibromas was probably due to their origin from anterior roots. The initial sensory disturbances in the form of paresthesias usually occurred in the upper extremities first. Twenty-four percent occurred first in the lower extremities. The first motor symptoms were in the upper extremities in 52 percent of the cases. In 35 of the 91 patients motor disturbances were first noted in the legs and feet. Quadriplegia was pres-

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ent in 41 cases. In 43 atrophy alone or atrophy with fibrillation was noted. There was definite loss of sensation in only 67. There was no anesthesia in only 9. In only 1 case there was no block or protein increase and this was a neurofibroma. Soltz and Jervis[6] in reporting on extramedullary tumors of the upper cervical cord found that the outstanding phenomenon was motor involvement. As in our case, the only sensory findings were the subjective ones. They found that the tumors were usually on the ventral or ventrolateral aspect of the cord involving pyramidal tracts and ventral horns. Sensory loss was variable and in a few cases no sensory change could be demonstrated. According to Tilney and Elsberg sensory disturbances at a distance from the level are due to a lamellar arrangement of the fibers in the spino-thalamic tracts. Fibers from the most caudal dermatomes lie more laterally within the sphere of influence of the compressing agent. They also noted that not infrequently sensory alterations appeared after operation. In our case there was some questionable hypalgesia over a patchy area in the lower left extremity. Disturbances in vibratory sense or position are disregarded in the diagnosis of upper cervical cord tumors. In fact such changes usually indicate intrinsic disease of the cord. Freedman[7] and Elsberg[1] observed postural disturbances of the neck and neck rigidity in cervical cord tumors. Our patient presented angulation of the head to one side with almost complete neck rigidity.

Case History: A 53 year old female was admitted to Ward 4 of the Cook County Hospital on January 8, 1948. The following history was obtained: On September 7, 1943, while talking over the telephone she was seized with a sharp pain over the thorax anteriorly. There was no radiation of the pain. A physician was called who made a diagnosis of a cardiac or a cerebral condition. The systolic blood pressure was found to be 220. Absolute bed rest was recommended for six to eight weeks. During that time weakness of the left lower extremity became apparent. There was progressive weakness of all four extremities so that by December 1945 she had lost complete use of the lower and upper extremities except for 10 degree flexion at the left elbow. For the past two years she had experienced muscular spasms especially in the lower extremities. For two months prior to hospitalization there were sharp stabbing pains in the right shoulder and mandible. No bladder or rectal disturbances were present at any time. Inventory by systems was negative. The past surgical history was negative except for an appendectomy in 1919 and a cholecystectomy in 1940. On July 23, 1947 she was admitted to the Mount Sinai Hospital where neurological examination revealed a bilateral hemiplegia without involvement of cranial nerves. There were exaggerated tendon reflexes and a bilateral Babinski and Rossolimo response on the left with no disturbances of sensation. No speech or bulbar disturbance was present. Extremities were spastic and resistive to passive movements. There were beginning contractures of the fingers. A spinal puncture revealed a clear colorless fluid which contained two cells, globulin two plus, and total protein 122 mg. percent. The gold curve was flat and the Wassermann negative. The dynamics were normal. A diagnosis of bilateral thrombosis of the middle cerebral arteries was made.

On admission to the Cook County Hospital the patient presented the following findings: The blood pressure was 240/140. She was mentally alert and cooperative. The cranial nerves and optic fundi were normal. The patient was unable to move any portion of the lower or right upper extremities. There was approximately 10 degrees range of flexion in the left elbow. There was a moderate degree of spasticity on the left side. There were no fibrillations. A slight atrophy of the thenar muscles was present bilaterally. All the deep tendon and periosteal reflexes were brisk, more so on the right side. There were bilateral Hoffman, Babinski, Chaddock and left Rossolimo responses with an unsustained left ankle clonus. The superficial abdominal reflexes were absent. All modalities of sensibility were intact. The head was held rigidly and it was tilted to the left. Lumbar puncture re-

vealed a clear fluid which contained no cells; the Pandy test was 4 plus; protein 280 mg. percent; glucose 93 mg. percent; colloidal gold curve 000111000; the Wasserman test was negative. The dynamics revealed absence of block. Compression of the left jugular produced a rapid rise in pressure from 100 mm. to 230 and a rapid fall to 110 when the pressure was released. Compression of the right jugular produced a rapid rise in pressure from 110 to 240 and a rapid fall to 110 when the pressure was released. X-rays of the cervical, thoracic and lumbar spines revealed only anterior lipping of dorsal vertebrae and the presence of a cervical rib on the right. X-rays of the skull revealed a moderate amount of hyperostosis internus frontalis. The foramen magnum was negative. Chest x-rays were normal. Gastric analysis revealed the presence of free acid. The blood count and hemoglobin were normal. Urine was negative. The non protein nitrogen was 41.

Impression: The history of a slowly progressive quadriplegia with a protein of 280 mg. per cent strongly suggested a neoplasm and with the absence of cranial nerve involvement, a high cervical lesion was considered. A laminectomy was advised and in this opinion we both concurred. When a cervical laminectomy was performed by one of us (HCV), a large dumbbell hourglass tumor was found at the level of the second invertebral space. The intraspinal portion of the tumor was anterior to the greatly attenuated cord which was estimated to be only 20 percent of its normal size. The tumor was removed without incidence although it was necessary to pack the extraspinal tumor cavity with gelatin sponge in order to control venous oozing. Microscopic examination of the tumor revealed it to be a typical neurofibroma.

Despite the long period of paralysis and the severely prolonged compression of the cord, the patient showed within six weeks, a surprising return of neurologic function. This case well demonstrates the difficulty of recognizing the space occupying lesions in the cervical portion of the spinal canal, especially so when they are located anteriorly to the spinal cord. It is astonishing that such a large intraspinal mass could exist without producing subarachnoid block which could be demonstrated by routine manometric studies at the time of spinal puncture. The elevation of the total protein (280 mg.) of the spinal fluid was the only real clinical clue to the presence of a tumor.

In retrospect we find it difficult to understand how we failed to recognize such a large tumor roentgenographically. However, the second and third cervical vertebrae were not satisfactorily recognized in the routine anterio-posterior roentgenogram of the cervical spine and review of the lateral film fails to reveal any significant bony change. The patient was obese with a short, thick neck and consequently the extraspinal portion of the growth was not recognized on routine physical examination. Contrast myelography did not seem advisable in such a high cervical lesion, as the patient's short thick neck would have made it difficult to hyperextend her neck sufficiently to prevent the contrast medium from entering the intracranial cavity when it was pooled in the upper cervical region. The results fortunately substantiated our clinical judgment in advising surgical exploration. After 8 months of postoperative treatment with physiotherapy, the patient was discharged from the hospital with almost complete return of function of the upper extremities in writing, sewing, typing, etc. She was able to walk alone on level ground and could climb stairs with the assistance of a rail.

Conclusion

This is a case of a 53 year old white woman with a progressive spastic quadriplegia of 4½ years' duration, with absence of disturbance of sensibility, negative roentgenographic findings and no subarachnoid block. The only strongly suggestive positive finding was the high spinal protein content. Surgery was performed without study with contrast media and substantiated our clinical impression of cord tumor. Excellent clinical recovery was made considering the duration of symptoms and extent of damage to the cord.

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Neurological Clinical Pathological Conference

of the

Cincinnati General Hospital

CHARLES D. ARING, M.D., *Editor*

Case No. 290071

Presentation

A 49-year-old housewife was admitted to the hospital November 16, 1948 with the complaint of intermittent pain in the left temporal region. Approximately 5 years previously she was awakened from sleep with severe cutting pain over the left zygomatic arch. It disappeared after a few days and recurred only occasionally during the following two years, being precipitated by talking or chewing. Since 1945 the pain had been more or less continuous. Medication and tonsillectomy were of no avail. The past history did not contribute with the exception that she had had rather severe left mastoid infection in 1925.

During the admission examination the patient had a bout of severe pain over the left zygoma which radiated backward toward the ear. Examination failed to reveal abnormality except for a point of exquisite tenderness 1 cm. in front of the left ear. Two per cent procaine injected into the left zygomatic region produced transient relief, whereas procaine and alcohol injection into the same area produced relief for 24 hours. On November 24 the left temporal artery and accompanying nerves were resected and the patient was discharged 4 days later.

Shortly after returning home she again began to experience the continuous, dull, aching pain over the left preauricular area, slightly worse than before; the sharp lancinating pains became much more frequent and severe. The pains were primarily in the preauricular area, but occasionally radiated to the temporal or parotid region. She was readmitted January 16, 1949 when examination revealed only sensory deficit in the region of the previous operative site. Pneumoencephalography prior to operation on January 17, 1949 failed to demonstrate an intracranial lesion; cerebrospinal fluid pressure was normal.

Blood pressure, pulse rate, respiratory rate, and temperature were normal. Blood counts, hemoglobin determinations, blood urea nitrogen and chlorides were normal, as was the urinalysis. The cerebrospinal fluid examination was normal.

Roentgen examination of the skull revealed the bones of the frontal area to be unusually thick but of normal density. The bones in the parietal and occipital areas were normal. Symmetrical heavy vascular markings were seen in the frontal and temporal areas. The sella turcica, petrous pyramids and sphenoidal fissure appeared normal.

Differential Diagnosis

Dr. Daniel Osher: One of the commoner problems confronting the physician is that of headache and head pain and although the vast majority of these complaints are due to benign causes either psychological or physiological, some may be due to serious physical disease requiring prompt diagnosis and treatment. Also, the benign forms

engender great suffering and anxiety and their proper diagnosis and therapy is important.

The various mechanisms of head pain have been investigated by Harold G. Wolff and his colleagues, and their monumental work[1] forms the basis for a logical and scientific attack on this complex problem. I will borrow freely from their work in the following discussion.

Head pain may arise from stimulation of pain fibers located in structures either inside or outside of the skull. Wolff found that the following structures are those within the cranium capable of giving rise to pain: the great venous sinuses and venous tributaries from the surface of the brain, parts of the dura at the base, the dural arteries and the cerebral arteries at the base of the brain. Thus the skull, the diploic vessels, the brain parenchyma, the ventricular lining and the choroid plexuses are insensitive to pain.

There are 6 basic intracranial mechanisms of headache production, (1) traction on veins going into the venous sinuses or displacement of the sinuses, (2) traction on large arteries at the base, (3) traction on the middle meningeal arteries, (4) distention and dilatation of intracranial arteries, (5) inflammation in or about any of the pain sensitive structures, and (6) direct pressure by tumors or adjacent lesions on the cranial and cervical nerves containing pain fibers.

Stimulation of pain sensitive structures on or above the tentorium results in pain in the anterior part of the head in front of a line drawn over the top of the head from ear to ear and on the same side of the head as the stimulated structure. This pain is carried by branches of the trigeminal nerve. Pain resulting from subtentorial stimulation will be referred to the back of the head and neck and is carried by the 9th and 10th cranial nerves and the upper 3 cervical nerves.

In brain tumor, headache is not primarily related to increased intracranial pressure but is due to traction on pain sensitive structures either by local traction of the tumor mass or distant traction by displacement of the brain.

Extracranial pain sensitive structures include the skin, galea, fascia, muscle and especially the arteries. The veins are probably not sensitive. The arteries are sensitive to dilatation and pressure but not to constriction. Wolff believes that dilatation of various arteries of the scalp and face underlie most of the transient recurring face and head pains including such conditions as migraine, hypertensive headache, and the complex group of atypical facial neuralgias. The cause of this arterial dilatation is not known but is related to periods of psychological stress and is often a part of generalized physiological disturbances. The pain is usually of a throbbing aching character and often associated with vasomotor changes such as visible dilatation of the vessels, redness of the skin, conjunctival injection, lacrimation, and nasal discharge. The patient is usually free of pain between attacks.

Diseases of the teeth, nose, sinuses, eyes and ears form another large group of causes of head and face pain. The pain is usually most intense at the site of disease but is frequently referred along branches of the 5th nerve or in mastoid disease to the posterior part of the head and neck. This pain is of a dull aching nature without throbbing or nausea and vomiting such as occurs in vascular types of pain.

In response to many of the above types of pain there occurs secondarily a reflex contraction of the scalp and neck muscles which if sustained will give rise to cramp-like aches, feelings of tightness, tenderness, crawling sensations and hyperalgesia overlying the muscles involved. More commonly these muscle tension pains and headaches occur in emotionally tense, aggressive, frustrated and anxious people.

Head and face pain can be due to lesions of the nerves themselves. Thus we have the major neuralgias or painful tics, inflammations of the nerves and pressure on the nerves either mechanical or due to tumors.

The most common of the major neuralgias is trigeminal neuralgia or tic douloureux. Characteristically this occurs in the older age group and consists of recurrent periods varying from a few days to several months during which there are frequent excruciating, brief (20-30 seconds) jabs of

pain in one or more divisions of the trigeminal nerve often associated with trigger zones but not with areas of anesthesia or motor weakness. There is freedom from pain between the paroxysms. A similar but much less common condition is 9th nerve or glossopharyngeal neuralgia with pain occurring in the tonsillar area and in the ear, usually brought on by swallowing. A third, very rare type is geniculate neuralgia with tic-like pain either in the ear or in front of the ear which can be relieved by section of the nervus intermedius.

Inflammations of various sensory cranial nerves most commonly caused by the herpes zoster virus can produce neuralgic pain. This type of pain is steady and not tic-like and has a burning, aching quality to it. It may last for weeks to months after the appearance of the vesicles along the course of distribution of the involved nerve but rarely lasts longer than a year. Late in the course of the disease, one finds scars of the vesicles and either hyperalgesia or more usually hypalgesia in the area of distribution of the nerve. When herpes zoster affects the geniculate ganglion of the 7th cranial nerve it is termed Ramsey Hunt syndrome; in it there are vesicles in the concha of the ear and facial palsy, deep facial pain and pain in the ear.

Tumors may infiltrate into or press upon various pain sensitive structures and nerves about the head and face and thus produce pain.

Finally, there are instances of head pain due to mechanical trauma or pressure upon nerves. Thus pain following lacerating injuries may be due to neuroma formation or scar tissue pressure on nerves. Bony hyperplasia as in tumors, Padget's disease and acromegaly may cause pain by compressing nerves as they pass through the various foramina. More recently Raney[2] described face and head pain due to herniated cervical disc. Falling into the group of mechanical irritation of nerves is a syndrome which I would like to discuss in detail, namely Costen's syndrome.

Costen, an otologist, about 15 years ago described pain and discomfort on chewing, with trismus, cracking noises in the temporo-mandibular joint during jaw movement, obscure neuralgias in and about the head, pain, tinnitus and deafness in the ear, all of which he believed were due to mandibular malposition usually occurring when molar teeth were missing. There are often changes demonstrable by x-ray in the temporo-mandibular joint and the symptoms are due to excessive movement of the mandibular condyle with resultant pressure on the articular branches of the auriculotemporal nerve or upon the nerve itself. This causes the pains over the joint and along the distribution of the nerve. The ear symptoms are the result of nervous and muscular changes in the eustachian tube and middle ear; often the drum is retracted. Relief of these symptoms results from correction of the abnormal joint movements by dental methods.

Now, as to the patient under discussion, intracranial causes of the pain have been ruled out by the lack of neurological findings plus the normal laboratory tests including pneumoencephalography. Vascular head pain such as occurs in migraine, hypertension and atypical facial pain gives an entirely different clinical picture than the one presented here. There is no evidence given in the protocol of tooth, sinus, eye or ear disease. This is obviously not one of the major neuralgias and there is no history of herpes zoster or other inflammatory nerve disease. Tumor causing nerve pain of this long duration would have surely revealed itself. I believe the x-ray changes in the skull are within normal limits and show no evidence of Paget's disease or acromegaly. A minimal degree of hyperostosis frontalis interna may exist but Wolff does not believe that this is a cause of headache. This is not the type of pain that occurs in tension headaches with sustained muscular contraction. There is no history of injury.

Thus we have a woman with constant pain in the area of distribution of the left auriculo-temporal nerve made worse on talking or chewing with marked tenderness in front of the ear either overlying the nerve or the temporo-mandibular joint, with x-ray evidence of absent molars—for that matter

all her teeth were gone—who was not relieved by cutting of the distal branches of the auriculo-temporal nerve. This all may add up to Costen's syndrome. The ear symptoms are a variable component of this picture. I do not know what operative procedure was done but the pain could be relieved by 5th nerve section or correcting the mandibular malposition. The brief lasting relief given by cutting the left temporal artery and accompanying nerves can be explained on two factors, psychological, in which any type of dramatic therapy may relieve pain, and physical, enforced rest of the diseased part caused by the pain from the operative incision and the hyperemia induced by the operation.

In passing I would like to make a few remarks about psychogenic headache. Many of the above described headaches although psychogenically induced are the result of physiological changes in vessels and muscles and thus are psychosomatic headaches. Psychogenic headache may consist of bizarre sensations in the head often termed burning, pricking or bandlike; it may vary in location, and is often more of a pressure sensation. In spite of the advances that have been made in the past few years in the understanding of various pain mechanisms about the head, these cases often remain confusing and perplexing problems.

Pathological Discussion

Dr. Joseph P. Evans: I assisted Dr. Shaver at the first operation on November 24, 1948. The left temporal artery and accompanying nerve was exposed in the left subtemporal region under local anesthesia. Dense scar tissue was found surrounding the entire artery with its major branches as it was thought at first that this might be due to the previous injection at this site. Following the removal of this tissue, it was noted that traction on nerves penetrating the temporal fascia caused exquisite tenderness and there was similar tenderness on pressure over the fascia in front of the auricle.

The fascia and muscle were then incised down to the underlying temporal bone and the muscle elevated therefrom. The outer table of bone showed numerous small areas of erosion occupied by small nubbins of tissue 2 to 3 mm. in diameter. This tissue was curretted away and saved for microscopic examination. At the time it was thought that some of these might represent mastoid air cells or might be the result of a chronic mastoiditis. The wound was closed in the usual manner and the healing occurred readily.

Dr. Murton R. Shaver: On microscopic examination dense areas of fibrous tissue extended around blood vessels and adjacent nerve fibers; there were some segments of temporal muscle present. There was very little inflammatory infiltration. Islands of round polyhedral cells grossly resembling those seen in arachnoidal villi were found scattered throughout the tissue extending into the muscle in some areas. Special stains failed to demonstrate the presence of collagen fibers and no mitotic figures were seen. It was thought that these areas of tissue might represent an extracranial extension of an intracranial meningioma (meningeal fibroblastoma).

Doctor Evans: Because of progression of symptoms the patient was re-explored on January 17, 1949. The former incision was reopened and the underlying bone removed. The tumor was almost missed as it lay posterior to the craniotomy just mesial to the temporal bone and extended mesially on the upper surface of the petrous bone. It measured approximately 3.5 x 2 x 2 cm. and was firmly attached to the underlying dura, which was not penetrated. The overlying bone was removed together with the tumor which was found to erode the surface of the petrous bone. This surface was then cauterized and the patient made an uninterrupted recovery following the operation.

The tumor mass was found to be firm, fibrous, and smooth in outline. The cut surface showed no areas of hemorrhage or necrosis and was rather fleshy in appearance.

Doctor Shaver: Sections of bone removed at this time together with sections of the tumor showed similar tissue to that described in the previous sections taken during the first operation. Sheets of these cells were found lying in the middle table of the bone and eroding the inner and outer ta-

bles. These extended outward into temporal muscle in some areas. The tumor itself showed similar cells arranged in sheets separated in some instances by fibrous septa with come collagen production. These cells again seemed to resemble very closely those seen in arachnoidal villi. They had a polyhedral appearance and showed some variation in size although they appeared on the whole rather uniform. The nuclei were large and in general there is very little collagen production. No mitotic figures were observed, Many of these sheets of cells appeared to be arranged in islands around the blood vessels but the latter were not exceedingly numerous in the tumor. There was no definite arrangement of the cells as seen in some types of meningioma where the collagen production is greater and the cells are arranged in whorls around blood vessels.

A diagnosis of meningioma (meningeal fibroblastoma) was made without difficulty on this tissue.

Clinical Diagnosis

Atypical facial pain with possible meningioma.

Dr. Osher's Diagnosis

Costen's syndrome.

Pathological Diagnosis

Meningeal fibroblastoma.

Dr. Osher: How is the patient now?

Dr. Evans: The pain was caused by direct involvement of the peripheral nerve and at present she is completely free of pain.

Dr. Norman Chivers: Did the radiologist think the vascular markings were worth remarking about?

Dr. Evans: There was no significance to them at all.

Dr. Osher: Frankly, I have never seen a patient with Costen's syndrome, but it seemed to fit this patient quite well. I did mention tumor in my discussion, but this is one type of intracranial tumor which does not produce the usual laboratory signs.

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